The Effectiveness of a Damage Control Resuscitation Strategy for Vascular Injury in a Combat Support Hospital: Results of a Case Control Study

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Objectives: Major vascular injury is a leading cause of potentially preventable hemorrhagic death in modern combat operations. An optimal resuscitation approach for military trauma should offer both rapid hemorrhage control and early reversal of metabolic derangements. The objective of this report is to establish the use and effectiveness of a damage control resuscitation (DCR) strategy in the setting of wartime vascular injury.

Methods: A retrospective two-cohort case control study was performed using the Joint Theater Trauma Registry to identify patients with an extremity vascular injury treated at two different points in time: group $1 \ (n = 16)$ from April to June 2006 when DCR concepts were put

into practice and group 2 (n = 24) 1 year later in a period when DCR strategies were not employed.

Results: Baseline demographics, injury severity, admission physiology, and operative details were similar between groups 1 and 2. Group 1 patients received more total blood products (23 vs. 12 units, p < 0.05), fresh frozen plasma (16 vs. 7 units, p < 0.01), cryoprecipitate (11 vs. 1.2 units, p < 0.05), whole blood (19% vs. 0%, p = 0.06), and early recombinant factor VIIa (75% vs. 0%, p < 0.001) than group 2 patients. Group 1 patients had a more complete early physiologic recovery after vascular reconstruction (heart rate: 38 vs. 12, p < 0.001; systolic blood pressure, 39 vs. 14, p < 0.001; base deficit: 7.36 vs.

2.72, p < 0.001; International Normalized Ratio, 0.3 vs. 0.1, p < 0.001). There was no significant difference in early amputation rates (group 1: 6.2% vs. group 2: 4.2%) or 7-day mortality (0% in both groups).

Conclusions: This study was the first to use the Joint Theater Trauma Registry for follow-up on an established clinical practice guideline. DCR goals appear now to be met during the management of acute wartime vascular injuries with effective correction of physiologic shock. The overall impact of this resuscitation strategy on long-term outcomes such as limb salvage and mortality remains to be determined.

Key Words: Vascular trauma, Damage control, Resuscitation, Coagulopathy.

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dvancements in combat casualty care have resulted in a significant reduction in mortality when compared with previous wars as current research has focused much attention on preventable death. Hemorrhage from extremity vascular injury remains a leading cause of potentially preventable death on the modern battlefield and

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recent estimates suggest an increase in this injury pattern compared with previous wars.^{2,3} Injuries of this severity cause an early and profound coagulopathy that is often present at admission to the emergency department (ED).^{4,5} Standard damage control principles are routinely applied to achieve rapid hemorrhage control, and to initiate a hemostatic resuscitation plan that will correct metabolic imbalances and prevent the onset or progression of a traumatic coagulopathy. Only when this lifesaving sequence is properly executed, can the military trauma patient be expected to withstand the metabolic perturbations of a complicated operation like extremity revascularization.^{6,7}

Standard surgical doctrine and experience has taught surgeons that the operative patient needs to be adequately resuscitated before embarking on a taxing operative course. ^{8,9} The time needed for adequate resuscitation was the single greatest barrier to limb salvage during the Korean conflict. ¹⁰ Convincing modern data show that acidosis and traditional resuscitation techniques using liberal amounts of crystalloid and packed red blood cells (PRBCs) can exacerbate coagulopathy. ^{11–14} One report has recently demonstrated a survival benefit with early correction of these physiologic derangements. ^{12,15} Given modern advances, it seems logical to optimize those strategies that promote early recovery from the metabolic consequences of hemorrhagic shock.

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Report Documentation Page

Form Approved OMB No. 0704-0188 Damage control resuscitation (DCR) is one such strategy that has been proposed for expedient correction of early physiologic imbalances and has been useful in our own experience for military vascular trauma. This employs the use of fresh whole blood (FWB), or a high ratio (≤1:1.4) of plasma to PRBCs, minimal crystalloid use, and liberal replacement of platelets, and cryoprecipitate. Early recombinant factor VIIa (rFVIIa) was used when indicated according to specific clinical practice guidelines.

Although evidence-based clinical guidelines for DCR have been established, their overall implementation and effectiveness have not been reported. The objective of this study was to assess the use and effectiveness of a DCR strategy in a case control study of combat-related vascular trauma. Additionally, this study aims to provide early insight into the impact of DCR on early limb salvage and survival.

PATIENTS AND METHODS

Using the Joint Theater Trauma Registry (JTTR), two cohorts of patients treated at different time periods for wartime vascular injury at a Baghdad-based US Combat Support Hospital (CSH) were created. Comparison of basic demographic, physiologic, resuscitation and early outcomes were compared between these cohorts. Group 1 (n = 16) consisted of wartime injured treated during the establishment of DCR clinical practice guidelines (April–June, 2006). Group 2 (n = 24) was comprised of patients with wartime vascular injury treated at a later time period when these guidelines were not followed (April–June 2007).

Included were those patients who arrived at the CSH with a life-threatening hemorrhage (>4 units PRBCs) from penetrating military munitions and underwent simultaneous saphenous revascularization for a pulseless extremity. Group 1 (DCR) patients received a resuscitation strategy that included early rFVIIA, FWB or PRBCs with a high plasma ratio (≤1:1.4), and minimal crystalloids. Group 2 did not receive FWB, rFVIIA, use high plasma ratios, or minimize crystalloid use. Patients with isolated cervical or torso vascular injury were not included unless they were associated with a pulseless extremity injury. Excluded were any arterial injuries that had thrombectomy and lateral suture or primary repair to re-establish a pulse as these repairs are not comparable to injuries that require a saphenous vein harvest for vessel reconstruction. The study was approved (Protocol Number Iraq 06-009) by the research committee of the participating CSH and the Brooke Army Medical Center Institutional Review Board.

Demographic data collection included patient gender, age, Injury Severity Score (ISS), and mechanism of injury. Physiologic data collection included the initial presenting vital signs (rectal temperature, blood pressure, heart rate) and physiologic parameters that included pH, base deficit, hemoglobin (g/dL), and International normalized ratio (INR). Operative blood product requirements to include those units received in the emergency room were documented. The

amount of transfused PRBCs, plasma, cryoprecipitate, and platelets were monitored. The doses of recombinant factor VIIa (rFVIIa) given were reported (typically $90-120 \mu g/kg$). Patients that required a massive PRBC transfusion (≥ 10 units), or FWB were noted.

After emergent extremity revascularization, the patient was taken to the intensive care unit (ICU) and the initial vital signs were observed. The ICU admission laboratory analysis included a postoperative complete blood count, arterial blood gas sample, and coagulation studies. The differences (Δ) in vital signs and lab study results obtained in the ED and the ICU were used to determine the extent of early physiologic recovery.

Primary outcome measures were normalization of the initial physiologic derangements, and a successful revascularization of the pulseless extremity as defined by restoration of a palpable pulse and establishment of a normal anklebrachial Index (>0.9). Early success was determined and reflected in 7-day survival, and amputation rate. Operative details including location of arterial injury, associated venous injury, type and configuration of conduit used, and procedure times were reviewed. Standard paired *t*-tests (continuous variables) or Fisher's exact test (percentage ratios) were used to determine statistical significance.

RESULTS

During the combined study periods 40 patients underwent arterial vascular reconstructions using a saphenous graft for 10 upper (25%) and 30 lower extremity (75%) wounds. The study group consisted of US service members (15, 38%) and Iraqi nationals (25, 62%). All but one patient was male with an age range of 18 years to 47 years. Baseline demographics and admission physiology (Table 1) were similar between both cohorts. The military ISSs and the operative times (23.6 \pm 9.6; 273 minutes \pm 98.7 minutes [group 1]) $(24.4 \pm 10.1; 266 \text{ minutes } \pm 89 \text{ minutes } [\text{group } 2]) \text{ were not}$ significantly different. Vessel injuries were all from penetrating trauma and consisted of high-energy explosions (18, 45%) or gunshot wounds (22, 55%). All vascular injuries were associated with large soft tissue wounds and fractures that required external fixation. Fasciotomy (25, 63%) was an accepted and routine practice. Because of the short prehospital transport time (\sim 30 minutes), extremity ischemic times were limited. Prehospital tourniquets (36 of 40, 90%) were used regularly. The technique of temporary shunt placement and delayed reconstruction (7, 18%) was used occasionally in both upper (3) and lower (4) extremity injuries to facilitate patient transfer from resource limited locations or when the patient condition was deteriorating.

Group 1: DCR

The response to resuscitation measures were reflected in early correction of presenting physiologic imbalances upon conclusion of the operative procedure for limb salvage. Table 2 demonstrates the degree of recovery in both cohorts. A comparison of physiologic differences from ED arrival (Ta-

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 Table 1
 Demographics and Averaged Physiologic Parameters on ED Arrival in Both Cohorts

Variable	All Patients (n)	Group 1 (DCR) (n)	Group 2 (n)	р
Age (yr)	25.3 ± 8.8 (36)	22 ± 5.1 (15)	27.6 ± 10.2 (21)	0.07
Injury of Severity Score	$22.9 \pm 9.1 (40)$	23.6 ± 9.6 (16)	24.4 ± 10.1 (24)	0.71
Glasgow Coma Score	$14.0 \pm 2.3 (35)$	$13.2 \pm 3.4 (12)$	14.4 ± 1.5 (23)	0.27
Systolic blood pressure	109 ± 31 (39)	105 ± 29 (15)	110 ± 32 (24)	0.64
Diastolic blood pressure	63 ± 23 (39)	60 ± 18 (15)	64 ± 26 (24)	0.58
Heart rate	121 ± 29.2 (39)	128 ± 24.3 (15)	117 ± 31.5 (24)	0.24
Temperature (°F)	98.7 ± 1.2 (34)	98.5 ± 1.3 (14)	98.7 ± 1.2 (20)	0.58
pH	$7.29 \pm 0.2 (39)$	7.27 ± 0.11 (15)	7.30 ± 0.2 (24)	0.64
Base deficit	$7.35 \pm 6.5 (40)$	$7.50 \pm 5.5 (16)$	$7.25 \pm 7.3 (24)$	0.91
Hb (g/dL)	$10.4 \pm 2.7 (40)$	$9.0 \pm 2.0 (16)$	$11.4 \pm 2.7 (24)$	0.005*
INR	$1.4 \pm 0.4 (40)$	$1.3 \pm 0.4 (16)$	1.4 ± 0.4 (24)	0.78

p values are derived from standard t-tests.

Data are mean ± SD unless otherwise specified.

Table 2 Physiologic Recovery After Vascular Reconstruction in 2 Cohorts ± DCR

Variable	Group 1 (DCR) (n)	DCR Δ	р	Group 2 (n)	No DCR Δ	р
OR time (min)	273 ± 99 (16)			266 ± 89 (24)		0.83
Systolic blood pressure	144 ± 27 (15)	39	0.001*	124 ± 28 (24)	14	0.11
Diastolic blood pressure	78 ± 13 (15)	18	0.005*	65 ± 17 (24)	1	0.93
Heart rate	90 ± 14 (15)	-38	<0.001 [†]	$105 \pm 26 (24)$	-12	0.07
Temperature (°F)	$98.5 \pm 0.7 (14)$	-0.09	0.86	98.4 ± 1.01 (20)	-0.3	0.19
рН	$7.39 \pm 0.06 (14)$	0.12	0.013*	$7.32 \pm 0.08 (17)$	0.02	0.34
Base deficit	$0.14 \pm 2.8 (14)$	7.36	<0.001 [†]	$4.53 \pm 3.9 (17)$	2.72	0.09
Hb (g/dL)	$11.3 \pm 2.3 (14)$	2.3	0.014*	$9.3 \pm 1.7 (24)$	-2.1	0.007
INR	1.0 ± 0.35 (13)	0.3	0.009*	1.5 ± 0.37 (24)	0.1	0.14

Data are mean ± SD unless otherwise specified.

ble 1) to ICU admission was made and determined by the change in vital signs and normalization of laboratory studies. Compared with group 2, patients who were treated in the earlier period using DCR (group 1) had a more complete early physiologic recovery After vascular reconstruction (HR: Δ HR 38 vs. 12, p < 0.001; Δ SBP39 vs. 14, p < 0.001and ΔBD : 7.36 vs. 2.72, p < 0.001). In group 1 systolic and diastolic blood pressure increased concordantly, and the heart rate decreased to a normal rate by the time the patient reached the ICU. Additionally, acidosis, coagulopathy, and anemia were all normalized at the time of ICU admission. This was determined by correction of pH, base deficit, INR, and hemoglobin derangements. These normalized values were significant (Table 2) when compared with baseline variables within the same group, and when compared with group 2 without a DCR strategy. Temperature was the only measure that was not statistically improved since patients arrived normothermic and remained so during the operative procedure.

Patients treated in the era of DCR (group 1) received more total blood products (23 vs. 12%, p=0.04) more fresh frozen plasma (FFP) (16 vs. 7 units, p<0.01), more cryo-

precipitate (11 vs. 1.2 units, p < 0.05), and whole blood (19%) vs. 0%, p = 0.06) than patients in group 2 treated without a DCR strategy. Total components given (65 vs. 21 units, p =0.004) was significantly more in the DCR group, although 14 patients (88%) required a massive transfusion, and this did not differ significantly from the 63% in group 2. FFP (given at 1:1.4) closely approximated a recommended 1:1 ratio with PRBCs but did not differ significantly from the FFP ratio of 1:1.7 in group 2.15 In the DCR group less crystalloid 1.6 vs. 3.01p = 0.02) was administered in the ICU. Most of these patients (12 of 16, 75%) received rFVIIa during the emergency room resuscitation with one to two additional doses (90-120 μg/kg) given intraoperatively. Because of the coagulopathic bleeding concerns heparin was not used (11, 69%) or only limited to a half dose (5, 31%). However, despite liberal use of rFVIIa and the limited use of heparin, none of the patients in this series had an early thrombotic graft failure. All patients survived the early postoperative period. The average transfusion requirements are summarized after DCR and compared with traditional resuscitation practices in Table 3.

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^{*} p < 0.05

ED indicates emergency department; Hb, hemoglobin; INR, international normalized ratio; DCR, damage control resuscitation.

Δ, Comparison of physiologic differences from ED arrival (Table 1) to ICU admission.

Vitals signs and lab studies were taken immediately at ICU admission.

p values are derived from standard paired t tests. (* p < 0.05, † p < 0.001) except OR time, which used standard t test.

Hb indicates hemoglobin; INR, international normalized ratio; DCR, damage control resuscitation; ED, emergency department; ICU, intensive care unit.

Table 3 Summary of Averaged 24-Hour Transfusion Requirements After Damage Control Resuscitation Compared With Traditional Resuscitation Practices (no DCR)

Blood Component	DCR	No DCR	p
Total blood products*	23 ± 18 units	12 ± 6.4	0.04
FFP	16 \pm 12 units	7 ± 5.6	0.01
Plasma: RBC ratio	1:1.4	1:1.7	0.16
Cryoprecipitate	11 \pm 14 units	1.2 ± 6.12	0.02
Platelets	13 \pm 9 units	0.7 ± 0.91	< 0.001
Total components	65 units	21 units	0.004
Total crystalloid	$7.1 \pm 3.2 L$	8.4 ± 3.4 L	0.31
ICU crystalloid	$1.6 \pm 1.0 L$	$3.0 \pm 1.8 L$	0.02
Massive transfusion (≥10 units)	88%	63%	0.15
rFVIIa (1 dose = $90-120 \mu g/kg$)	75%	0%	< 0.001
Whole blood (6 units)	19%	0%	0.06

^{*} Packed RBCs + whole blood.

Group 1: Vascular Techniques

Sixteen patients underwent emergent reconstruction for limb salvage for an arterial injury using an interposition vein graft (n = 10, 63%) with good muscle coverage or as a reversed saphenous vein bypass graft (n = 6, 37%) around the zone of injury. Repair of concomitant venous injury (n = 5, 31%) was favored, and none of the venous injuries in this group were ligated. Injuries occurred to the brachial, ulnar, femoral, popliteal, and tibial arteries. Bypass to distal tibial vessels (5) were performed in one third of the patients in this group. The median operative time required for these procedures was 273 minutes (range 1.7-8.4 hours). Included was the time spent for fasciotomy, vein harvest, external fixation and similar to group 2, may have been performed by a second surgical team. One amputation was performed for extensive soft tissue loss. There were no early graft failures or deaths in the first week. During transport a mechanical ventilator failure resulted in an anoxic brain injury and eventual death of one patient. Another patient with a penetrating colon injury died of abdominal sepsis. Both deaths occurred on POD8 from associated wounds that were unrelated to the vascular injury or the DCR. The distribution, management, and outcome of these vascular injuries are shown in Table 4. There was no significant difference in early amputation rates (group 1: 6.2% vs. group 2: 4.2%) or 7-day mortality (0% in both groups) between groups (Table 5).

Group 2: Traditional Resuscitation

Demographics with averaged physiologic parameters on ED arrival (Table 1) and a comparison of resuscitation outcomes are summarized in Table 2. In group 2 using a traditional resuscitation strategy both the systolic and diastolic blood pressure did not significantly change between the ED and the ICU. Patients remained tachycardic (HR: 105), and the change over time (Δ 12, p=0.07) was not significant. Additionally, acidosis (base deficit) although improved, remained relatively uncorrected (-7.25 to -4.53 post pro-

cedure, $\Delta 2.72$, p = 0.09). Anemia and coagulopathy as measured by Hb, and INR were worsened at the time of ICU admission and were discordant when compared with the results achieved in the DCR group. None of the variables demonstrated significant ($p \le 0.05$) reversal of metabolic derangements when analyzed by paired t test. Hemoglobin,

Table 4 Location of All Vascular Injuries and Type of Surgical Treatment Performed

_					
Location/Artery	Total (n = 40)	Group 1 (DCR) (n = 16)	Venous*	Group 2 (n = 24)	Venous*
Upper extremity					
Axillary	1			1	
Brachial	8	2 ^{†(1)}		6	
Ulnar	1	1			
Lower extremity					
Femoral	13	5	4/4	8	5/6
Popliteal	10	3	1/1	7 ^{†(3)}	2/4
Tibial	7	5 ^{†(4)}		2†(2)	
Total	40	16	5/5	24	7/10 [‡]

Saphenous vein interposition graft unless otherwise specified.

DCR indicates damage control resuscitation.

Table 5 Outcomes of Each Treatment Group With Respect to Complications

Variable	All Patients (n = 40)	Group 1 (DCR) (n = 16)	Group 2 (n = 24)	р
Early graft failure (%)	2.5	0	4.17	1*
Temporary shunting (%)	17.5	25	12.5	0.41*
Amputation (%)	5	6.25	4.17	1*
Seven day mortality (%)	0†	0†	0	

^{*} Fisher's exact test.

DCR indicates damage control resuscitation.

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FFP indicates fresh frozen plasma or thawed plasma; RBC, red blood cells; DCR, damage control resuscitation; rFVIIa, recombinant factor VIIa.

^{*} Concomitant vein injury and repair.

^{† (}n) Reversed saphenous bypass graft.

[‡] Venous ligation = 3/10.

[†] Two deaths on POD8.

the only variable that differed from group 1 in the ED, decreased from an average 11.4% to 9.3% (p = 0.007).

Averaged 24-hour blood product requirements show that 15 (63%) patients required a massive transfusion. Component therapy was the standard for blood product transfusions and no patients had FWB administered. Crystalloid resuscitation averaged 8.3 L, not significantly more than group 1 but consisted of a greater amount given in the ICU (3.0 vs. 1.6 L p=0.02). Thawed or fresh frozen AB plasma was given less deliberately (1:1.7 ratio) when compared with the plasma (1:1.4 ratio) used in the DCR group. In contrast to the DCR group, none of the patients in group 2 received rFVIIa. Heparin was used frequently (21, 88%). These average transfusion requirements are summarized after DCR and compared with traditional resuscitation practices in Table 3.

Group 2: Vascular Techniques

Twenty-four vascular reconstructions for limb salvage were performed in group 2 using an interposition vein graft (n = 19, 79%) or as a reversed saphenous vein bypass graft (n = 5, 21%) around the zone of injury. Repair of concomitant venous injury was preferred in 7 of 10 cases. There were two popliteal venous injuries and one femoral venous injury that were ligated at the time of arterial repair. The only documented amputation was performed on a popliteal arterial injury with venous ligation. Injuries occurred to the axillary, brachial, femoral, popliteal, and tibial arteries. Bypass to distal tibial vessels (2, 8.3%) were less frequent when compared with the experience of group 1 (5, 31%). The median operative time required for these procedures were 266 minutes and ranged from 2.0 hours to 9.2 hours. The location of all vascular injuries and the type of surgical treatment performed is shown in Table 4. The outcome of each treatment group with respect to complications is detailed in Table 5.

DISCUSSION

This study represents the first to use the JTTR to provide follow-up on the use and effectiveness of an established clinical care guideline. DCR goals seem to be met during the management of acute wartime vascular injuries with effective correction of physiologic shock. The overall impact of this resuscitation strategy on long-term outcomes such as limb salvage and mortality remain to be determined although results from this study are encouraging.

Arterial injury accounted for a significant number of the amputations performed in combat casualties during World War II. Time lapses between wounding and treatment together with the inability to preserve circulation contributed to a very high rate of limb loss at that time. ¹⁶ Priority evacuation during the Korean War reduced this time lag to 4 hours, however, an additional 6 hours was often spent in preparing patients for surgery. Severe blood loss and demand for complete resuscitation often became so time consuming that amputation was unavoidable. This wartime experience eventually taught that "rushing the improperly resuscitated patient

to surgery in an attempt to save a limb may possibly result in the loss of life." ¹⁰ Experienced surgeons now stress the importance of avoiding these delays by emphasizing that a majority of resuscitative activities can be accomplished simultaneously in the operating room. ⁹

Modern research has focused on developing resuscitation strategies that serve to reverse those classic physiologic derangements that often lead to death. 17 Predicting the need for massive transfusion, need for a lifesaving intervention or mortality based on vital signs, and presenting physiologic parameters like INR or base deficit can avoid undue delay and justify effective resuscitation plans. 4,18-21 "Staying out of trouble, rather than getting out of trouble" is an indispensable concept in damage control surgery because hemorrhagic deaths after injury typically occur within 2 hours to 4 hours. Early hemorrhage control and hemostatic resuscitation are critical components to the successful management of a vascular injured patient. We previously reported a DCR strategy that can facilitate early hemostasis, restore physiology, and quickly normalize metabolic derangements during a simultaneous extremity vascular reconstruction in conjunction with rapid surgical intervention.⁶ Reluctance for some to implement DCR strategy for vascular trauma seems to be based in speculative concerns on the increased risk of graft thrombosis when coagulopathy is aggressively treated. The objective of this project was to examine the effectiveness of a DCR strategy for vascular trauma in a CSH by performing a retrospective twocohort case control study. This analysis is important because hemorrhagic shock is observed in approximately 25% of combat-related injuries.7 One third of these patients were coagulopathic and, based on coagulopathy or acidosis, these patients have physiologic derangement incompatible with a time consuming vascular reconstruction.^{8,22,23} Combining the concepts of DCR with expeditious limb salvage may advance the immediate surgical management of extremity vascular injuries.

Establishing resuscitation goals are important as combat wounded who present in shock have high mortality. In a review of US casualties in Baghdad, patients with an INR >1.5 and decreased platelets at admission had a mortality of 30% compared with 5% when the INR was normal. 11 Prothrombin time is an established independent risk factor for mortality, and certain other risk factors have been correlated with the development of a life-threatening coagulopathy.⁵ Cosgriff et al. showed that 98% of hypothermic patients with an ISS >25 that presented with acidosis and hypotension developed a coagulopathy.²⁴ Increased severity of clinical acidosis is found to be associated with increased mortality and, although little is known about the underlying mechanisms, there is general agreement that acidosis can also worsen coagulopathy and may have a profound inhibitory effect on thrombin generation. 11,25

Avoiding dilutional coagulopathy has been well described for elective vascular cases. Waters established that the increased use of saline in patients undergoing abdominal aortic aneurysm repair resulted in significantly more blood

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products being used, suggesting a harmful effect on the coagulation system.²⁶ Kiraly et al. also showed that saline produced a relative hypocoagulable state after trauma and increased blood loss.²⁷ Resuscitation with crystalloid fluid has also been linked with the development of worsening acidosis, which is then related to worsening coagulopathy. By minimizing crystalloid, one prevents further dilution of deficient clotting factors and iatrogenic injury.²⁸ Alternatively, liberal use of plasma instead of crystalloids can help prevent acidosis and dilutional coagulopathy, whereas the use of tris-hydroxymethylaminomethane (Tham) can correct intracellular respiratory and metabolic acidosis.^{13,15,25}

DCR concepts have gained momentum as Hirshberg et al. showed that exsanguinating trauma patients should receive FFP with the first units of PRBCs to circumvent further hemodilution, and based on computer simulation, recommended a ratio of 2:3.²⁹ Many other recent published reports now exist and strongly recommend equal ratios of plasma and packed cells and platelets to achieve a physiologic composition comparable to FWB. 13,15,30-32 FWB often used in combat hospitals, has been shown to correct dilutional coagulopathy with evidence that a single unit has the hemostatic effect of 10 units of platelets. 33,34 Additionally, one retrospective analysis cited a 39% relative risk reduction in mortality that was noted in a group of combat casualties who were given FWB.11 Transfusion recommendations are often developed from elective surgery protocols and may not be applicable to combat casualties. The first study to support the concept that early and aggressive replacement of coagulation factors may improve survival by decreasing death from shock has led to a recent policy change from the Office of the Army Surgeon General for the current theater of operations. Borgman et al. demonstrated that the ratio of blood products transfused was associated with mortality in patients receiving a massive transfusion at a CSH.¹⁵ Numerous investigators have called for increased plasma and criticize traditional transfusion strategies.35-37

The use and benefits of rFVIIa for trauma have been described previously. $^{38-46}$ In the management of isolated extremity trauma, rFVIIa was used sparingly and reserved for cases when hemorrhage was not surgically treatable or controlled with hemostatic dressings. The Central Command (CENTCOM) Clinical Practice guideline called for IV administration of 90 $\mu g/kg$ to 120 $\mu g/kg$ rFVIIa given first in the ED, with additional doses given intraoperatively to treat acquired coagulopathy and reduce hemorrhage. 47 The goal of these interventions was a normal INR in the operating room and to that end the goal was achieved.

The use and effectiveness of the proposed DCR strategy in the setting of wartime vascular injury was dramatic. Using DCR, early physiologic recovery from shock while in the operating room was demonstrated by all measured variables. This was particularly the case for physiologically distressed patients that were given FWB. These patients often had a normal heart rate, blood pressure, and evidence of systemic coagulation within the first hour of the operative procedure.

Specifically heart rate and blood pressure was normal at the time of ICU admission. Likewise, liberal use of plasma resulted in a normal coagulation profile upon ICU arrival. Although the plasma to RBC ratio did not differ significantly between groups, the overall use of plasma remained significantly higher in the DCR group. The preferred use of blood products over crystalloid resuscitation in the DCR group was reflected in the final hemoglobin concentration, as hemodilution was avoided and the need for additional fluids in the ICU was significantly less when compared with those without DCR. The averaged total blood component for the DCR group was significantly higher and probably underscores the need to replace the lost blood volume in patients suffering from hemorrhagic shock from vascular wounds. Although admission physiology, demographics, and operative details were similar, half (12 of 24) of the patients in group 2 arrived in the ICU with an uncorrected coagulopathy (INR >1.5). The cohort without DCR arrived in the ICU tachycardic, with no significant changes noted in blood pressure. Hemoglobin concentration in group 2 was the only variable that differed significantly because it declined from 11.4 g/dL to 9.3 g/dL. In contrast, the DCR group hemoglobin improved from 9.0 g/dL to 11.3 g/dL. In group 2, acidosis as reflected in the base deficit only improved from -7.25 to -4.53. The immediate physiologic improvements using DCR concepts seem evident and may favor continued implementation of DCR clinical care guidelines. The overall impact of this resuscitation strategy on long-term outcomes such as limb salvage and mortality remain to be determined although early outcomes with respect to complications should not discourage or limit DCR specifically for vascular trauma.

The small number of patients, short observation period, and retrospective design are obvious limitations of this project. Despite the limitations, the findings of this study are novel and have merit. For example, this report demonstrates the ability of the JTTR to develop an evidence-based clinical guideline and to provide follow-up of this guideline later in time. This accomplishment in itself is important and serves as a model for future wartime clinical care. Additional aspects of the data in this report are especially compelling and corroborate studies in the civilian trauma literature and point to value of DCR in wartime. Although all DCR guidelines have not fully been met, there are distinct trends in this direction. The effectiveness of this strategy lies in the observation that in groups that had equal physiologic disturbances upon presentation to the CSH, there was a more effective restoration of heart rate, and blood pressure during the earlier cohort (group 1) in which DCR was used. Additionally, this report demonstrated that despite high total blood components, patients treated in the era of DCR had aggressive early correction of acidosis, anemia, and coagulopathy without an increase in early graft failure. We anticipate with future JTTR data and refined use of a DCR strategy, that benefits to combat casualties with vascular injury will be identified over time.

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CONCLUSION

This study represents the first to use the JTTR to provide follow-up on the use and effectiveness of an established clinical practice guideline. DCR goals seem now to be met during the management of acute wartime vascular injuries with effective correction of physiologic shock. The data show excellent early survival and limb salvage with an amputation rate of 4% to 6%, regardless of the resuscitation practices used. Aggressive DCR maneuvers do not result in early graft failures and yet permit complex extremity revascularization with simultaneous improvements in the physiologic condition at the conclusion of the vascular operation. Comprehensive long-term graft surveillance is necessary to establish formal conclusions regarding the durable repair of vascular injuries.

Given the number of recent reports that demonstrated a higher mortality associated with massive transfusion, earlier death from shock, and increased mortality when coagulopathy is uncorrected, immediate correction of a traumatic coagulopathy should not be discouraged for vascular surgery. We encourage DCR as an effective resuscitation strategy for all combat-related vascular injuries. The overall impact of this resuscitation strategy on long-term outcomes such as limb salvage and mortality remain to be determined.

REFERENCES

- Eastridge BJ, Jenkins D, Flaherty S, Schiller H, Holcomb JB.
 Trauma system development in a theater of war: experiences from
 operation Iraqi freedom and operation enduring freedom. *J Trauma*.
 2006;61:1366–1372.
- Holcomb JB, McMullin NR, Pearse L, et al. Causes of death in US Special Operations Forces in the global war on terrorism 2001–2004. Ann Surg. 2007;245:986–991.
- Rasmussen TE, Clouse WD, Jenkins DH, Peck MA, Eliason JL, Smith DL. Echelons of care and the management of wartime vascular injury: a report from the 332nd EMDG/Air Force Theater Hospital, Balad Air Base, Iraq. Perspect Vasc Surg Endovasc Ther. 2006;18:91–99.
- Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. J Trauma. 2003;54:1127–1130.
- MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M. Early coagulopathy predicts mortality in trauma. *J Trauma*. 2003;55: 39–44.
- Fox CJ, Gillespie DL, Cox ED, et al. Damage control resuscitation for vascular surgery in a combat support hospital. J Trauma. In press.
- Beekley AC, Watts DM. Combat trauma experience with the United States Army 102nd Forward Surgical Team in Afghanistan. Am J Surg. 2004;187:652–654.
- Porter JM, Ivatury RR, Nassoura ZE. Extending the horizons of "damage control" in unstable trauma patients beyond the abdomen and gastrointestinal tract. *J Trauma*. 1997;42:559–561.
- Aucar JA, Hirshberg A. Damage control for vascular injuries. Surg Clin North Am. 1997;77:853–862.
- Hughes CW. Arterial repair during the Korean war. Ann Surg. 1958; 147:555–561.
- Tieu BH, Holcomb JB, Schreiber MA. Coagulopathy: its pathophysiology and treatment in the injured patient. World J Surg. 2007;31:1055–1065.
- Holcomb JB, Jenkins D, Rhee P, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. *J Trauma*. 2007;62:307–310.

- Hess JR, Holcomb JB, Hoyt DB. Damage control resuscitation: the need for specific blood products to treat the coagulopathy of trauma. *Transfusion*. 2006;46:685–686.
- Kauvar DS, Holcomb JB, Norris GC, Hess JR. Fresh whole blood transfusion: a controversial military practice. *J Trauma*. 2006; 61:181–184.
- Borgman MA, Spinella PC, Perkins J, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma*. 2007;63: 805–813.
- DeBakey ME, Simeone MC. Battle injuries of the arteries in World War II: an analysis of 2,471 cases. *Ann Surg.* 1946; 123:534–579.
- Sagraves SG, Toschlog EA, Rotondo MF. Damage control surgery the intensivist's role. J Intensive Care Med. 2006;21:5–16.
- Holcomb JB, Salinas J, McManus JM, Miller CC, Cooke WH, Convertino VA. Manual vital signs reliably predict need for lifesaving interventions in trauma patients. *J Trauma*. 2005;59: 821–828.
- 19. Eastridge BJ, Malone D, Holcomb JB. Early predictors of transfusion and mortality after injury: a review of the data-based literature. *J Trauma*. 2006;60:S20–S25.
- Davis JW, Shackford SR, Mackersie RC, Hoyt DB. Base deficit as a guide to volume resuscitation. *J Trauma*. 1988;28:1464–1467.
- Moore FA, McKinley BA, Moore EE, et al. Need for massive transfusion can be predicted early after trauma center arrival. *J Trauma*. In press.
- Damage Control Surgery. In: Burris D, Fitzharris JB, Holcomb JB, et al, eds. *Emergency War Surgery*. Washington, DC: Borden Institute; 2004:12.1–12.10.
- Starnes BW, Beekley AC, Sebesta JA, Andersen CA, Rush RM Jr. Extremity vascular injuries on the battlefield: tips for surgeons deploying to war. *J Trauma*. 2006;60:432–442.
- Cosgriff N, Moore EE, Sauaia A, Kenny-Moynihan M, Burch JM, Galloway B. Predicting life-threatening coagulopathy in the massively transfused trauma patient: hypothermia and acidoses revisited. *J Trauma*. 1997;42:857–861.
- Martini WZ, Dubick MA, Wade CE, Holcomb JB. Evaluation of tris-hydroxymethylaminomethane on reversing coagulation abnormalities caused by acidosis in pigs. *Crit Care Med.* 2007; 35:1568–1574.
- Waters JH, Gottlieb A, Schoenwald P, Popovich MJ, Sprung J, Nelson DR. Normal saline versus lactated Ringer's solution for intraoperative fluid management in patients undergoing abdominal aortic aneurysm repair: an outcome study. *Anesth Analg.* 2001; 93:817–822.
- Kiraly LN, Differding JA, Enomoto TM, et al. Resuscitation with normal saline (NS) vs. lactated ringers (LR) modulates hypercoagulability and leads to increased blood loss in an uncontrolled hemorrhagic shock swine model. *J Trauma*. 2006; 61:57–64
- 28. Alam HB, Rhee P. New developments in fluid resuscitation. *Surg Clin North Am.* 2007;87:55–72, vi.
- Hirshberg A, Dugas M, Banez EI, Scott BG, Wall MJ Jr, Mattox KL. Minimizing dilutional coagulopathy in exsanguinating hemorrhage: a computer simulation. *J Trauma*. 2003;54:454–463.
- Dutton RP, Carson JL. Indications for early red blood cell transfusion. *J Trauma*. 2006;60:S35–S40.
- Ketchum L, Hess JR, Hiippala S. Indications for early fresh frozen plasma, cryoprecipitate, and platelet transfusion in trauma. *J Trauma*. 2006;60:S51–S58.
- Malone DL, Hess JR, Fingerhut A. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. *J Trauma*. 2006;60:S91–S96.

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- Mohr R, Goor DA, Yellin A, Moshkovitz Y, Shinfeld A, Martinowitz U. Fresh blood units contain large potent platelets that improve hemostasis after open heart operations. *Ann Thorac Surg*. 1992;53:650-654.
- Lozano ML, Rivera J, Gonzalez-Conejero R, Moraleda JM, Vicente V. Loss of high-affinity thrombin receptors during platelet concentrate storage impairs the reactivity of platelets to thrombin. *Transfusion*. 1997;37:368–375.
- Hewson JR, Neame PB, Kumar N, et al. Coagulopathy related to dilution and hypotension during massive transfusion. *Crit Care Med*. 1985;13:387–391.
- Ho AM, Karmakar MK, Dion PW. Are we giving enough coagulation factors during major trauma resuscitation? Am J Surg. 2005;190:479 – 484.
- Gonzalez EA, Moore FA, Holcomb JB, et al. Fresh frozen plasma should be given earlier to patients requiring massive transfusion. *J Trauma*. 2007;62:112–119.
- Holcomb JB. Use of recombinant activated factor VII to treat the acquired coagulopathy of trauma. J Trauma. 2005;58:1298–1303.
- Holcomb JB, Hoots K, Moore FA. Treatment of an acquired coagulopathy with recombinant activated factor VII in a damagecontrol patient. *Mil Med.* 2005;170:287–290.
- Holcomb JB. Methods for improved hemorrhage control. Crit Care. 2004;8(suppl 2):S57–S60.
- Klemcke HG, Delgado A, Holcomb JB, et al. Effect of recombinant FVIIa in hypothermic, coagulopathic pigs with liver injuries. *J Trauma*. 2005;59:155–161.
- McMullin NR, Kauvar DS, Currier HM, Baskin TW, Pusateri AE, Holcomb JB. The clinical and laboratory response to recombinant factor VIIA in trauma and surgical patients with acquired coagulopathy. *Curr Surg.* 2006;63:246–251.
- Mohr AM, Holcomb JB, Dutton RP, Duranteau J. Recombinant activated factor VIIa and hemostasis in critical care: a focus on trauma. Crit Care. 2005;9(suppl 5):S37–S42.
- Schreiber MA, Holcomb JB, Rojkjaer R. Preclinical trauma studies of recombinant factor VIIa. Crit Care. 2005;9(suppl 5):S25–S28.
- White CE, Schrank AE, Baskin TW, Holcomb JB. Effects of recombinant activated factor VII in traumatic nonsurgical intracranial hemorrhage. *Curr Surg.* 2006;63:310–317.
- Perkins JG, Schreiber MA, Wade CE, Holcomb JB. Early versus late recombinant factor VIIa in combat trauma patients requiring massive transfusion. *J Trauma*. 2007;62:1095–1101.
- CENTCOM CPG. Recombinant factor VIIa [database on the Internet]: US Department of Defense. 2007. Available at: https://jpta.fhp.osd.mil.

DISCUSSION

Dr. Paul R. Cordts (Health Policy and Services, Office of the Surgeon General, Falls Church, VA): Dr. Fox et al. have conducted a retrospective study that seeks to answer the question: does Damage Control Resuscitation (DCR) have a negative impact on major vascular repairs? They compare two groups: 20 patients per group, 62% host national patients, similar ISSs, patients equally coagulopathic, and acidotic at admission. Patients in group 1 (DCR) were aggressively resuscitated with early use of rFVIIa (when indicated), fresh whole blood (FWB), transfusion of packed red blood cells (PRBCs) to fresh frozen plasma (FFP) in high ratios (approaching 1:1; generally for patients receiving massive transfusion ≥10 units PRBCs), and minimal crystalloid. The group 1 goal was early correction of physiologic derangements present at admission. Patients in group 2 underwent

traditional resuscitation strategies, with no FWB, more crystalloid use, less liberal use of FFP. No rFVIIa was used in group 2 vs. 64% of patients in group 1, although group 1 had more patients requiring massive resuscitation. Heparin use was more frequent in group 2. Vascular repairs with autogenous vein were similar in each group; venous repairs were less frequently performed in group 2. There were no perioperative deaths or early (within 1 week) vascular graft failures in either group. One amputation occurred in both groups. The authors conclude that DCR does not negatively impact early graft patency and, given this fact and the low amputation rate, that immediate correction of traumatic coagulopathy, even when vascular repair is required, should not be discouraged.

I commend Dr. Fox and his group for reassuring us that aggressive correction of coagulopathy does not seem to negatively affect early vascular graft patency, although this is a retrospective review with a small number of patients and relatively short observation period (the authors acknowledge this). Certainly this goes against traditional teaching, which may be to leave patients "thin," or slightly hypocoagulable, after major vascular surgery. I do agree that more long-term surveillance would be required to draw formal conclusions about vascular repairs, although one would think that most thrombotic complications would occur within 24 hours to 48 hours of surgery. I have four questions for Dr. Fox:

- 1. Outcome of venous repairs was not evaluated in your study. Would venous repairs be more susceptible to thrombosis than arterial repairs and would repairing a vein influence your decisions regarding DCR and use of heparin? Would the location (e.g., brachial, femoral, popliteal) of a venous repair make a difference?
- 2. Patients undergoing primary or lateral repairs with thrombectomy were excluded from your study, but would these other types of arterial repair influence your decision to use DCR? Would use of prosthetic graft influence your decision and is there any indication to place prosthetic grafts today?
- 3. One would think use of rFVIIa would be of particular concern with a fresh vascular repair. How did you decide to use it and was it useful, in your view?
- 4. Why the difference in resuscitation techniques between the two Combat Support Hospitals? Did this difference pertain to all trauma patients or only those patients undergoing major vascular repair?

Again, I congratulate these authors for exploring this important question. You have shown us that life and limb can be saved simultaneously and that patients can be effectively resuscitated highly in the OR and emerge with their coagulopathy corrected and a vascular repair which remains patent.

Dr. Charles J. Fox (Walter Reed Army Medical Center, Washington, DC): Thank you Dr. Cordts for the very insightful comments and excellent questions. Regarding venous injury, I think limb edema is probably an under appreciated morbidity.

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However in emergencies, most venous injuries can be successfully ligated, and the long-term durability of these repairs are difficult to determine in these circumstances. DCR is reserved as a strategy to correct life threatening physiology and should be used selectively for patients who need it without regard to the specific type of vascular injury that needs repair.

For the purpose of this study, we wanted to analyze a population that by historical data have high mortality from hemorrhagic shock, and need proper intraoperative resuscitation to withstand a lengthy extremity revascularization. Because lateral repairs do not have the same complexity as saphenous grafting, we purposely excluded them. But again, the patient's condition drives the resuscitation plan, not necessarily the type of injury.

Prosthetic graft use is controversial. There are a number of well done civilian series that advocate its use in clean wounds without risk of osteomyelitis. In contaminated extremity wounds with smaller vessels, vein grafts have superior patency. I have used prosthetic grafts for carotid and subclavian injuries with good results. I would not change my resuscitation strategy to suit the repair, prosthetic or vein. In fact I would promote just the opposite message . . . fix the injury, fix it well, and trust that your patient doesn't need to be coagulopathic for the graft to work.

I acknowledge that factor 7 is controversial. In our experience, it did not result in early graft failures. It has a very short half-life, and works at the site of tissue injury. Injured

arteries should be carefully debrided back to healthy tissue, with a carefully constructed anastomosis. Please note that we did not use factor 7 in all of our patients. Specifically, for those with isolated extremity injuries, particularly when a MT is not required, I would hold off, and even advocate for the use of some heparin. One should not think of DCR as an "all or none" event, it's more like a recipe . . . and all of the ingredients may not be essential, in all patients, all of the time.

Last, regarding differences in techniques, living on the tip of the spear in Baghdad allows us to see what current technology has done for our capability. To compare, in WWII only 81 repairs were performed on 2,471 patients. This led Dr. DeBakey to conclude that ligation was the best and probably only accepted way to manage a vascular injury during wartime. Drs. Spencer and Hughes challenged that thinking and as a result, reduced the amputation rate dramatically during the Korean War. Dr. Rich and others during the Vietnam War improved on those results by fixing venous injuries and forming a registry for future studies. Now, in Iraq, we are saying that the presenting physiologic condition that has classically led us to perform damage control surgery and amputation may no longer be a contraindication to complex or prolonged extremity vascular reconstruction when DCR principles are employed. Thank you very much for your attention. I thank the program committee for the opportunity to give this presentation today.

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